PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

NEUROSEARCH A/S
Patent Department
93 Pederstrupvej
DK-2750 Ballerup
DANEMARK

PV 27 JULI 2004

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	02.07.2004
Applicant's or agent's file reference 220-204-WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK 03/00539	13.08.2003	22.08.2002

Applicant
NEUROSEARCH A/S et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Ullrich, J Tel. +49 89 2399-8048

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 220-204-WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/DK 03/00539	International filing date *(day/month/year)* 13.08.2003	Priority date *(day/month/year)* 22.08.2002
International Patent Classification (IPC) or both national classification and IPC C07D471/04, C07D487/04, C12P41/00, C07D307/20		
Applicant NEUROSEARCH A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.02.2004	02.07.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Boletti-Cremers, K Telephone No. +49 89 2399-8541

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK 03/00539

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-16 as originally filed

Claims, Numbers

1-9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	7,9
Inventive step (IS)	Yes:	Claims	1-6
	No:	Claims	7-9
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations

   see separate sheet

POINT V.

The following documents , quoted in the I.S.R., have been considered as relevant for the examination of the present application . Their numbering will be adhered to for the rest of the procedure.

(1) WO-A- 98 14447 , cited in the application
(2) WO-A-01 18231.
(3) EP-A-0 439 779 , cited in the application.

1. Novelty.

1.1 In view of the fact that the process on file merely differs from the content of (1) (refer especially to page 13 line 16 to page 14, line 7 of (1)) by the use of a specific chiral α-N,N-diBoc-aminoxy-γ-butyrolactone for the obtention of the desired chiral end product , namely the compounds of type A or B , the claimed matter can be regarded as novel with respect to the content of (1).

1.2 (2) (refer especially to example 7 of (2), refer also to claims 1 and 3 of (2)) does not disclose the making of the chiral compounds A or B , but discloses the preparation of the starting material useful for the purpose of the preparation of the chiral γ-butyrolactone involved in the preparation of the chiral compounds A and B and as such , affects the novelty of claims 7 and 9 even if those claims refer on claims 1-6 .
Since the end products of claims 7-9 are the (S) or (R) enantiopure α-hydroxy-γ-butyrolactone , which are not the chiral α-N,N-diBoc-aminoxy-γ-butyrolactone which are used in claim 1, the reference to claims 1-6 as mentioned directly or not in claims 7 and 9 cannot be interpreted as a dependence and as such claim 7 has to be considered as an independent claim and claims 8 and 9 as dependent on claim 7 only. Nevertheless , the content of (2) does not affect the novelty of the other claims on file.

1.3 The same conclusions as for (2) can be drawn from the content of (3) which discloses a process to prepare the (R) and (S) enantiomers of α-OH-γ-butyrolactone (see example 1 of (3)) but not the making of the claimed chiral compounds A or B. Consequently to the preceding , claims 7 and 9 lack novelty , whereas the other claims not.

2. Inventiveness.

As can be seen from the contents of the documents quoted above , the preparation of the chiral isomers (compounds A and B) is neither disclosed nor suggested and as such , claims 1-6 are inventive , whereas claims 7-9 lack inventiveness because , even if rendered novel , they are based upon analogy with respect to the content of (2) and (3).

3. Formal points.

4.1 For the sake of clarity and in the regional proceedings to come , it might be preferable to insert a clear definitions of all the compounds involved by present processes as well as clear definitions of the transformation steps which link those compounds to each other in the text of the claims.

4.2 Document (2) should be mentioned and briefly discussed in the description when the application will reach the regional European proceedings.

POINT IV.

Lack of unity.

The Applicant is already warned that he will face a non unity objection in the regional proceedings because , as stands and as can be deduced from the previous points , present application deals "de facto" with 2 different problems which are not linked to each other by the same inventive concept , namely to provide chiral enantiomers of the compounds of type A and B by means of the process of claims 1-6 or to provide (possibly) a new synthetic path for the known (R) and (S) enantiomers α-OH-γ-butyrolactone of (2) and (3).